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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/723,594	11/26/2003	Yuan-Ping Pang	07039-161002	7578

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EXAMINER	
NEGIN, RUSSELL SCOTT	
ART UNIT	PAPER NUMBER
1631	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	01/17/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/723,594	PANG, YUAN-PING	
	Examiner	Art Unit	
	Russell S. Negin	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 October 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-18 and 25-72* is/are pending in the application.

4a) Of the above claim(s) *1-18 and 25-36* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *37-72* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *10/20/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Comments

Claims 37-72 are examined on the merits in the current Office action.

It is also noted that cancelled claims 19-24 should not contain text:

[see 37 C.F.R. 1.121(c)(4)].

Information Disclosure Statement

The Information Disclosure Statement filed 20 October 2006 corrects for the deficiencies in the IDS filed on 19 March 2004.

Specification

The objections to the disclosure are withdrawn due to amendments made by the applicant to the specification on 20 October 2006.

Claim Rejections - 35 USC § 112

The rejection of claims 37-72 under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a metal ion composed of a single atom, does not reasonably provide enablement for a polyatomic metal ion is withdrawn due to amendments made by the applicant to the set of claims filed on 20 October 2006.

The rejection of claims 37-72 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which

applicant regards as the invention is withdrawn due to amendments made by applicant to the set of claims filed on 20 October 2006.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 52, 53, 70 and 71 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 52, 53, 70 and 71 are indefinite because they list values of charge without assigning a sign (negative or positive) to the value.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

35 U.S.C. 103 Rejection #1:

Claims 37-47, 49-65, and 67-72 are rejected under 35 U.S.C. 103(a) as being unpatentable over Huheey et al. [Inorganic Chemistry, Fourth Edition, 1993, HarperCollins College Publishers] in view of Marchi et al. [Journal of Physics: Condensed Matter, volume 2, 1990, pages 5833-5848] as evidenced by Crawford [CH186 Lecture Presentation: Transition Metal/Coordination Chemistry accessed at

http://chemistry.semo.edu/crawford/ch186/lectures/ch20/index.html on 5 January 2007, last updated on 25 February 1999].

Claims 37 and 55 are the machine and computer readable media for performing molecular dynamics simulations of monoatomic metal ions attached to dummy atoms.

Claims 38-39 and 56-57 limit claims 37 and 55, respectively, to dummy atom masses.

Claims 40-43 and 58-61 limit claims 37 and 55, respectively, to shapes of the complex.

Claims [44-47, 49] and [62-65, 67] limit claims 37 and 55, respectively, to species of metal ions to be used.

Claims 50-51 and 68-69 limit claims 37 and 55, respectively, to comparisons of empirical and computational solvation energies.

Claims 52-54 and 70-72 limit claims 37 and 55, respectively, to charge values of dummy atoms.

On pages 397-399 of Huheey et al., Huheey et al. give details on crystal field theory. Specifically, Huheey et al. explain Crystal Field Effects for octahedral symmetry. Figure 11.6 on page 397 of Huheey et al. illustrates the model of crystal field theory for a monoatomic metal with a finite radius and black ligands. For examples of radii of monoatomic metals, see page 292 of Huheey et al. For examples of metal complexes to be utilized in crystal field theory, see Table 11.6 on page 406 on Huheey et al. The ligands fit the criteria for mass and charge for "dummy atoms," as stated in the instant claims. (i.e. Iron has a charge of +2 and a mass of 56 g/mol, fulfilling the requirements

of the instant claims). The metals in Table 11.6 of Huheey et al. include iron (a transition metal). Figure 11.15 on page 410 of Huheey et al. includes calcium and zinc as having a role in crystal field theory.

Furthermore, Figure 11.10 of Huheey et al. illustrates a tetrahedral configuration for crystal field theory with the ligands as black and white circles at the apices of the polyhedron, and the metal at the center of the representation.

Huheey et al. uses the term "ligands" instead of "dummy atoms." In addition, Huheey et al. does not conduct molecular dynamics simulations on a computer or computer readable medium with the complexes. Huheey et al. does not measure the energy of solvation of the metal ions as well.

Dummy atoms are defined in the specification on page 7, lines 29-30 as "an atom that is assigned a van der Waals size of zero. That is, a dummy atom is basically a point charge."

In the online lection of Crawford, Crawford states in slide 39 of 60, that crystal field theory "treats ligands as point negative charges." Consequently the description of ligands of Huheey et al. is synonymous with the definition of "dummy atom" in the instant specification.

The article of Marchi et al., entitled, "Solvation and ionization of alkali metals in liquid ammonia: a path integral Monte Carlo study," states in the first sentence of the abstract, "Quantum path integral Monte Carlo calculations have been used to study the properties of the alkali atoms Li, Na, and Cs immersed in liquid ammonia."

Molecular dynamics simulation details are discussed in section 3.2.1. on page 5836 of Marchi et al. Furthermore, the acknowledgments on page 5848 of Marchi et al. mentions that a computer system was used to carry out the simulation.

In the simulations of Marchi et al., the metal atom interacts with the surrounding ammonia molecules. Section 4.2. of Marchi et al., states as a result, "In all cases, the calculated PIMC electron total energy for the isolated atom matched the experimental value within a few per cent."

It would have been obvious to someone of ordinary skill in the art at the time of the instant invention to modify the crystal field theory discussed in Huheey et al. as evidenced by the definition of ligand of Crawford in view of the computer molecular dynamic simulations of Marchi et al., because Marchi et al. conducts simulations and measurements on analogous metal ion complexes than those discussed in Huheey et al. with the advantages of computer automation and analysis of the energetics of a solvent with the metal in solution to study the properties of alkali atoms (Li, Na, Cs) immersed in liquid ammonia.

35 U.S.C. 103 Rejection #2:

Claims 37, 48, 55, and 66 are rejected under 35 U.S.C. 103(a) as being unpatentable over Huheey et al. as evidenced by Crawford in view of Marchi et al. as applied to claims 37-47, 49-65, and 67-72 above, and further in view of Maggiora [Journal of the America Chemical Society, volume 95, 1973, pages 6555-6559].

Claims 48 and 66 limit the possible metal ion to magnesium.

Huheey et al. as evidenced by Crawford in view of Marchi et al. do not show use of magnesium as a metal ion.

The study of Maggiora, entitled, "Electronic structure of porphyrins. All valence electron self-consistent field molecular orbital calculations of free base, magnesium, and aquomagnesium porphines,"

The first full sentence of column 2 of page 6555 of Maggiora states, "Ground state properties are examined, and particular emphasis is placed on examination of the MO structure, electron populations, net atomic charges, metal-ligand bonding, and the importance of magnesium d orbitals to the bonding." As shown in the slide of Crawford, crystal field theory relies on the presence of the d orbitals of a metal.

It would have been obvious at the time of the instant invention for someone of ordinary skill in the art to modify Huheey et al. as evidenced by Crawford in view of Marchi as applied to claims 37-47, 49-65, and 67-72 above in further view of Maggiora because Maggiora shows how magnesium can possess d orbitals useful in the crystal field theory for binding the ligands (dummy atoms). Consequently, it would have been obvious for magnesium to be included in the ions disclosed in Huheey et al.

Conclusion

No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP

§ 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the central PTO Fax Center. The faxing of such pages must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993)(See 37 CFR § 1.6(d)). The Central PTO Fax Center Number is (571) 273-8300.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Russell Negin, Ph.D., whose telephone number is (571) 272-1083. The examiner can normally be reached on Monday-Friday from 7am to 4pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's Supervisor, Andrew Wang, Supervisory Patent Examiner, can be reached at (571) 272-0811.

Information regarding the status of the application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information on the PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

RSN
8 January 2007

RSN
8 January 2007

JOHN S. BRUSCA, PH.D
PRIMARY EXAMINER

Client Ref.: 07039-161002

Applicant : Yuan-Ping Pang
Serial No. : 10/723,594
Filed : November 26, 2003
Title : MOLECULAR MODELING FOR METALLOPROTEINS

Art Unit : 1631
Examiner : Russell Scott Negin
Conf. No. : 7578

RESUBMISSION OF MISSING REFERENCES

Examiner Initial	Desig. ID	Document as Resubmitted
RSN	AE	Aqvist et al., J. Am. Chem. Soc., 1990, 112(8):2860-2868
	AF	Atassi et al., Critical Reviews in Immunology, 1999, 19(3):219-260
	AG	Boehm et al., Biochem. Biophys. Res. Commun., 1998, 252:190-194
	AH	Braga et al., Chem. Commun., 1996, N5:571-578
	AI	Charifson et al., J. Computational Chem., 1991, 12(7):899-908
	AJ	Cieplak et al., J. Comp. Chem., 1995, 16(11):1357-1377
	AK	Cornell et al., J. Am. Chem. Soc., 1995, 117(19):5179-5197
	AL	El Yazal et al., J. Phys. Chem. B, 1999, 103:8773-8779
	AM	El Yazal et al., J. Phys. Chem. B, 2000, 104:6662-6667
	AN	Guilbaud et al., J. Phys. Chem., 1993, 97:5685-5692
	AO	Hanahan et al., Cell, 1996, 86(3):353-364
	AP	Hoops et al., J. Am. Chem. Soc., 1991, 113(22):8262-8270
	AQ	Klimpel et al., Mol. Microbiol., 1994, 13(6):1093-1100
	AR	Lu et al., Proteins, 1998, 33:119-134
	AS	Mackay et al., Trends Biochem. Sci., 1998, 23:1-4
	AU	Pang et al., J. Am. Chem. Soc., 1999, 121(8):1717-1725
	AV	Pang, J. Mol. Model., 1999, 5:196-202
	AW	Roe et al., J. Mol. Model., 1999, 5:134-140
	AX	Ryde, Proteins, 1995, 21:40-56
	AU	Santos et al., Clin. Exp. Metastasis, 1997, 15:499-508
	AZ	Schneider et al., Pure & Appl. Chem., 1993, 65(11):2329-2334
	AAA	Shalinsky et al., Annals of Oncology, 1998, 9(2):73, Abstract No. 278
	ABB	Shalinsky et al., Clin. Cancer Res., 1999, 5(7):1905-1917
	ACC	Sivaraja et al., J. Am. Chem. Soc., 1992, 114(9600-9603
	AEE	Vanhooke et al., Biochem., 1996, 35(19):6020-6025
	AFF	Vedani et al., J. Am. Chem. Soc., 1990, 112(12):4759-4767
	AGG	Vu et al., Cell, 1998, 93(3):411-422
	AHH	Wasserman et al., Proteins, 1996, 24(2):227-237
	AII	Zahn et al., J. Am. Chem. Soc., 1999, 121(32):7279-7282

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/Russell S. Negin/

01/05/2007